REMARKS

Claims 113, 115-121, 123, 125, 128-135, 137-139, 141-144, 170-175 and 177-183, 185, 187, and 190-239 constitute the pending claims in the present application. Claims 210-234 have been withdrawn as being directed to non-elected inventions.

Support for the amendments can be found throughout the instant specification and claims as filed, for example, at paragraph 1 of page 21, at page 32, at lines 25-27 of page 40, at lines 1-12 of page 24, and Example 1. Applicant asserts that no new matter has been added to the specification or claims. Applicant reserves the right to prosecute any canceled subject matter in a future application.

Applicant respectfully requests reconsideration of the rejections of record in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Formal matters

1. Applicant acknowledges the Examiner's withdrawal of claims 210-234.

2. Applicant acknowledges recordation of the Terminal Disclaimer filed on January 4, 2002.

Objection to the Specification

3. The specification was objected to for reciting "lose" at line 12 of page 18 because of a grammatical error.

As indicated above, Applicant has amended the specification to correct the grammatical error such that the specification now recites "low" at line 12 of page 18. Support for this phrase can be found throughout the specification as filed, such as at line 17 of page 18 and does not constitute new matter.

35 USC § 112, second paragraph

4. Claims 113, 126-127, 174, and 188-189 are rejected under 35 USC § 112, second paragraph, as allegedly being indefinite because:

(a) dependent claims 126-127 and 188-189 further characterize the binding agents as having been exposed to radiation; and

(b) claims 141, 170, 197, and 206 encompass binding reagents that have been exposed to radiation in that they are drawn to any imaging reagent, *e.g.*, radioisotopes.

In order to expedite the prosecution of this case, Applicant has canceled claims 126, 127, 188, and 189, thereby obviating the rejection with respect to these claims.

Applicant, however, would like to respectfully draw the Examiner's attention to the notion that radiolabels and irradiation are not equivalents. One of ordinary skill in the art would reasonably understand that the process of radiolabeling a protein encompasses combining a chemical molecule and a protein such that the protein is radioactive. Such well known radiolabels include ^{32}P, ^{131}I, and yttrium.

Irradiation, however, encompasses exposing a protein to a light source, such as an ultraviolet light bulb, without physical manipulation. The light source emits waves of varying lengths and results in a mutation to the existing protein. The mutation either reduces or alters the original protein's properties and does not involve addition of a chemical reagent to the protein.

Thus one of ordinary skill in the art would recognized that radiolabeling a protein and irradiating a protein are distinct processes. However, to expedite prosecution of the claims, Applicant has amended claims 141, 170, 197, and 206 to remove the limitation of "one or more imaging reagents", thereby obviating the rejection with respect to these claims.

Applicant reserves the right to pursue any canceled subject matter in a future application and respectfully requests reconsideration and withdrawal of the rejection.

35 USC § 112, first paragraph

5. Claims 113, 122-125, 135, 140, 174, 184-187, 201 and 205 are rejected under 35 USC § 112, first paragraph, as allegedly failing to enable one skilled in the art to make and/or use the invention.

The Examiner states at paragraph 2 of pages 5 of the Office Action that "[t]he claims are not enabled because there is insufficient guidance and objective evidence to predictably enable one of ordinary skill in the art to administer murine monoclonal antibodies (such as B43.13) in the absence of HAMA-induced toxicity in a **human** host." Based upon the teachings on page 49 of the specification wherein "when patients received more than one injection [of B43.13] and patients developed high amounts of human anti-mouse antibodies (HAMA), the antibody showed rapid clearance to liver and spleen)". Further, the Examiner cites Madiyalakan et al. (*Hybridoma*, Vol. 14, Number 2, 1995, pages 199-203) as teaching "that a large majority of patients developed isotypic HAMA upon injection of the monoclonal B43.13".

Applicant asserts that because the only claims drawn to administering murine monoclonal antibodies (such as B43.13) in the absence of HAMA-induced toxicity in a host are claims 124, 140, 186, and 205, the remaining claims (i.e., 113, 122-123, 125, 135, 174, 184, 185, 187, and 201) are fully enabled and should not have been rejected under 35 USC § 112, first paragraph for lack of enablement.

Applicant has canceled claims 124, 140, 186, and 205, solely to further prosecution of the remaining claims, thereby obviating the rejection. Applicant reserves the right to pursue any canceled subject in a future application and respectfully requests reconsideration and withdrawal of the rejection.

35 USC § 102(e)

6. Claims 113, 115-123, 128, 131-135, 141-144, 170-175, 177-185, 190, 193-204, 2-6-209 are rejected under 35 USC § 102(e) as allegedly being anticipated by U.S. Patent No. 5,997,315 (Chatterjee et al., the "'315 patent").

The '315 patent teaches a murine anti-idiotypic antibody, "3H1", which is an Ab2 antibody (see, for example, lines 29-31 of column 18, and lines 7-9 of column 19 of the '315 patent). In order to make 3H1, the mouse anti-CEA monoclonal antibody (8019) was conjugated to KLH, emulsified in Freund's adjuvant, and "was administered repetitively into the recipient animals on an unusual schedule with only two weeks between doses. Substantial responses only arose in about three mice only after the fourth immunization" (see lines 32-52 of column 18 of the '315 patent).

Column 2 describes Ab2 molecules which effectively mimic the structure of the tumor associated antigen identified by the Ab1 (see lines 5-7 of column 2 of the '315 patent) and indicates that a promising approach to cancer employs an "antibody mimicking an epitope of a tumor-associated protein [that] is administered in an effort to stimulate the patient's immune system against the tumor, via the tumor-associated protein" (see lines 25-30 of column 2 of the '315 patent). While it is true that the '315 patent discloses administration of an Ab1 antibody to a mouse that binds the CEA antigen at a first epitope, the immune response produced to that binding occurrence was to the same first epitope of CEA, not a second altered epitope. The Ab2 antibody (i.e., 3H1) that was produced and subsequently administered to a different mouse does not bind a first epitope on the antigen as required by Applicant's claims as Ab2 antibodies mimic the antigen. Therefore, the '315 patent does not teach the functional limitation of the binding agent of the instant claims wherein the binding agent binds "to a first epitope on the antigen..." and the immune response is "elicited against a second epitope on the antigen...".

Indeed, the '315 patent only teaches administration of an Ab2 antibody which mimics the antigen. It does not teach or suggest a therapeutic immune response from administration of a

binding agent that binds to a first epitope on an antigen and produces an effective immune response against a second epitope on the same antigen.

Not only does the '315 patent not teach or suggest that a binding agent that binds a first epitope and elicits a response against a second epitope could be used as a therapeutic tool, the Ab2 antibody taught in the '315 patent required multiple injections of Ab1 antibodies conjugated to KLH emulsified in Freund's adjuvant to make it immunogenic. Additionally, the 3H1 Ab2 antibody disclosed in the '315 patent is a hybridoma generated *ex vivo*.

In contrast, Applicant's binding agent administered at a low dose, with or without an adjuvant, can induce a therapeutic host response.

Claims 141, 170, 197, and 206 have been amended to remove the limitation that the binding agent is associated with one or more imaging agents.

Consequently, Applicant asserts that the '315 patent does not anticipate the claims as currently amended and respectfully requests reconsideration and withdrawal of the rejection.

35 USC § 102(b)

7. Claims 113, 115-123, 125-126, 129-135, 141-144, 170-185, 187-188, 191-204, and 206-208 are rejected under 35 USC § 102(b) as allegedly being anticipated by Madiyalakan et al. (Hybridoma, 1995, 14(2): 199-203) for the reasons of record in Paper No. 14.

The Examiner states at page 8 of the office action (Paper No. 26) that the rejection of record has been maintained "due to the apparent discrepancy in the claimed subject matter with regards to exposure to radiation. See 112, second paragraph rejection above".

Applicant assert that the Madiyalakan et al. pubication is not available as prior art under 35 USC § 102(b) because it was not published more than one year prior to the filing date of the instant application. The present application is a CIP of PCT/IB96/00461, filed on May 15, 1996, and claims priority to the same. Support for the claims in the present application can be found through out the specification of the parent application. Madiyalakan et al. was published on May 19, 1995 as evidenced in a letter from the publisher herewith submitted as Attachment A.

Therefore, the reference was not published more than one year prior to the filing date and thus may not be used as a 35 USC § 102(b) reference.

35 U.S.C. § 102 requires that each and every limitation of the claim be taught by the reference in order to anticipate the claimed invention.

Applicant asserts that as the rejection was based on the 112, second paragraph rejection set forth above, the 102b rejection should have been set forth only with respect to dependent claims 126, 127, 188 and 189 as the remaining claims do not encompass a radiolabeled antibody.

Applicant's position with respect to radiolabels and irradiation has been discussed *supra* with respect to the rejection under 35 § USC 112, second paragraph.

Nevertheless, Applicant has canceled claims 126, 127, 188, and 189, and has amended claims 141, 170, 197, and 206, solely to expedite prosecution of the remaining claims, thereby obviating the rejection for the reasons set forth herein, as well as for the reasons of record.

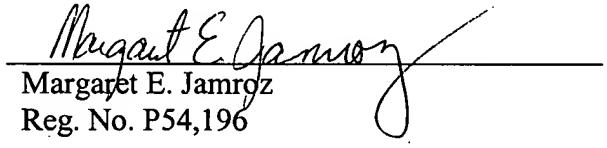
Applicant respectfully requests reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

Date: June 26, 2003



Margaret E. Jamroz
Reg. No. P54,196

Customer No: 28120
Docketing Specialist
Ropes & Gray, LLP
One International Place
Boston, MA 02110
Phone: 617-951-7000
Fax: 617-951-7050

Mary Ann Liebert, Inc. publishers
TWO MADISON AVENUE, LARCHMONT, N.Y. 10538

Tel: (914) 834-3100
FAX Tel: (914) 834-____

Appendix A
09/376,604
AREX-P03-004

February 7, 2002

Ms. Susan Mulvaney
Altarex Corporation
610 Lincoln Street
Waltham, MA 02451

Dear Ms. Mulvaney:

As per your request, please note the following information:

The publication date for HYBRIDOMA, VOLUME 14, NUMBER 2 is MAY 19, 1995.

Should you need any further assistance, please do not hesitate to contact me.

Sincerely,

Esther Bicovny